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(54) IMPROVEMENTS IN OR RELATING TO EXTRACTING ALKALOIDS FROM ERGOT OF RYE

(71) We, LEK TOVARNA FARMACEVTSKIH IN KEMICNIH IZDELKOV, a Yugoslavian Body Corporate, of Celovska c. 135, Ljubljana, Yugoslavia,

do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to a process for the isolation of alkaloids from the ergot of rye.

When isolating the ergot-alkaloids, their decomposability and conversion into inactive isomers has to be taken into account. For this reason the process should be accomplished rapidly, in order that the large quantity of ballast substances, mainly fats, do not effect the process.

Prior art procedures utilize a preliminary purification, e.g. extraction. This prolongs the reaction times, but causes considerable losses of alkaloids and undesirable isomerisation.

More recent processes omit the preliminary extraction. However, this has numerous other drawbacks. Whether the exrtacts are concentrated or various additives are used to prevent the formation of emulsions, the alkaloids are exposed to the action of heat and various reagents. The removal of the ballast substances requires a repeated transfer of the alkaloids from one solvent into another which prolongs the isolation procedure, lowers the yield and reduces the quality of the product.

The process according to the invention as hereinafter exemplified avoids the above-mentioned drawbacks to a high degree. The preliminary extraction is not necessary and separation of the alkaloids from the ballast substances proceeds easily and rapidly.

According to the present invention there is provided a process for the isolation of ergot-alkaloids which process comprises extracting ground ergot of rye with an organic water-immiscible solvent, contacting the resultant extract with an adsorbent material in order to reversibly adsorb the alkaloids, desorbing the alkaloids by means of a solvent which is more polar than the solvent used for the extraction, concentrating the resultant eluate *in vacuo* and thereafter precipitating the alkaloid by the addition of petroleum ether.

The drug is extracted with an organic, water-immiscible solvent, such as: chloroform, benzene, trichloroethylene, toluene, methylene chloride, or dichloroethane. The extract is filtered through a column of a suitable adsorbent, preferably alumina, whereby the alkaloids and small quantities of the ballast substances are adsorbed, whereas the greater part of the ballast substances are transferred into the filtrate. The adsorbed alkaloids are then eluted with a much smaller quantity of a more polar solvent or a mixture of the above-mentioned solvents with methanol or ethanol. Subsequently the eluate is concentrated to $^1/_{20}$ of its volume and separated from the major part of the ballast substances remaining on the adsorbent. The alkaloids are isolated from the eluate by careful evaporation of the solvent *in vacuo* and precipitation in an excess of petroleum ether. The process of adsorption and desorption of the alkaloids can be followed in UV-light. The same effect is attained by suspending the adsorbent in the extract or eluate and separating it by filtration.

The process according to the invention is illustrated in detail by the following example:

EXAMPLE

10 kg. of ground ergot of rye is extracted in the usual manner with trichloroethylene. 50 litres of the extract ia passed through two 75 g. columns of active alumina over a period of 2 hours .The active alumina is contained in two glass columns with a diameter of 10 cm. and a length of 50 cm. The alkaloids are eluted with 2 litres of ethyl acetate and the eluate is concentrated to a volume of about 150 cc. The alkaloid-bases are precipitated by pouring the concentrate into a tenfold quantity of petroleum ether filtered off and dried in a vacuum drier.

The yield amounts to 90% of the alkaloids

contained in the drug, in the form of a whitish amorphous powder containing 85 to 90%, with respect to the ergotamin-base. The percentage of the dextrorotatory isomers is practically the same as in the drug.

WHAT WE CLAIM IS:—

1. A process for the isolation of ergot-alkaloids which process comprises extracting ground ergot of rye with an organic water-immiscible solvent, contacting the resultant extract with an adsorbent material in order to reversibly adsorb the alkaloids, desorbing the alkaloids by means of a solvent which is more polar than the solvent used for the extraction, concentrating the resultant eluate *in vacuo* and thereafter precipitating the alkaloid by the addition of petroleum ether.

2. A process as claimed in claim 1 wherein the organic-water immiscible solvent is chloroform, benzene, trichlorethylene, toluene, methylene chloride or dichloroethane.

3. A process as claimed in claim 1 or claim 2 wherein the adsorbent material is alumina.

4. A process as claimed in any of the preceding claims wherein the solvent used to desorb the alkaloid is ethyl acetate.

5. A process as claimed in any one of claims 1 to 3 wherein the solvent used to desorb the alkaloid is a mixture of the organic water-immiscible solvent and methanol or ethanol.

6. A process for the isolation of ergot-alkaloids as claimed in claim 1 substantially as described herein in the foregoing example.

7. Ergot-alkaloids whenever isolated by the process as claimed in any one of the foregoing claims.

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